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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/798,766	03/11/2004	Francois Maltais	2004993-0011 (VPI/03-101)	8361
27916 7590 08/16/2007 VERTEX PHARMACEUTICALS INC. 130 WAVERLY STREET CAMBRIDGE, MA 02139-4242			EXAMINER KOSACK, JOSEPH R	
			ART UNIT 1626	PAPER NUMBER
			MAIL DATE 08/16/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/798,766	Applicant(s) MALTAIS ET AL.	
	Examiner Joseph Kosack	Art Unit 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 April 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12,14,15,17 and 18 is/are pending in the application.
- 4a) Of the above claim(s) 8,15,17 and 18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7,9-12 and 14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-12, 14-15, and 17-18 are pending in the instant application.

Election/Restrictions

Applicant is reminded that as per MPEP 803.02, when a provisional election of species is found to be unpatentable, then the provisional election will be given effect. However, if and when the elected species is found to be allowable, the search will be expanded to include additional species. Additionally 68 distinct species does not constitute a reasonable number and would impose a serious burden upon the Examiner. Applicant has stated that a complete search has been done on the corresponding PCT application. This is immaterial because applications go through a different restriction practice internationally and are not restricted based on the independent and distinct standard. Finally, claim 1 is a *Markush* claim and not a linking claim. A linking claim is drawn to a class of compounds not defined in the alternative. Claim 1 is defined in the alternative language of a Markush claim.

The restriction requirement is maintained as FINAL.

Previous Claim Objections

Claims 1-7 and 9-14 were previously objected to for containing elected and non-elected subject matter. As non-elected subject matter is still in the claims, the objection is maintained. Applicant is reminded that once the elected species is found to be allowable, the scope of elected subject matter will be expanded to cover additional species. The objection is withdrawn for claim 13 as that claim has been cancelled.

Previous Claim Rejections - 35 USC § 103

Claims 1-7 and 9-14 were previously rejected under 35 U.S.C. 103(a) as being obvious over Cao et al. (USPN 6,743,791) in view of In re Wood (199 USPQ 137). Applicant's statement under 35 U.S.C. 103(c) as disqualified Cao et al. as prior art and the rejection is withdrawn.

Previous Double Patenting Rejections

Claims 1-7 and 9-14 were previously rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2 and 22-23 of U.S. Patent No. 6,743,791 in view of In re Wood (199 USPQ 137).

Additionally, claims 1-7 and 9-14 were previously provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 20 and 41-42 of copending Application No. 10/770,814, published as US-PGPUB 2004/0229875 A1 in view of In re Wood (199 USPQ 137) and Patani et al. (*Chemical Reviews* 1996, 3147-3176).

At the time of this action, the terminal disclaimers that have been filed on April 11, 2007 have not been approved by the office. Therefore, the rejections will be maintained until the approval of the terminal disclaimers. The rejection of claim 13 is dropped as that claim has been cancelled.

Claims 1-7 and 9-14 were previously provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 22-23 of copending Application No. 11/128,870, published as US-PGPUB 2006/0106069 A1 in view of In re Wood (199 USPQ 137) and Patani et al. (*Chemical Reviews* 1996, 3147-3176). As a rejection remains on the instant application, the

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provisional rejection will be currently maintained. The rejection is withdrawn for claim 13 as it has been cancelled.

Claim Objections

Claims 1-7, 9-12, and 14 are objected to for containing elected and non-elected subject matter. The elected subject matter have been identified supra.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

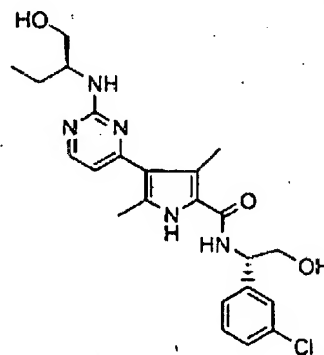
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

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consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

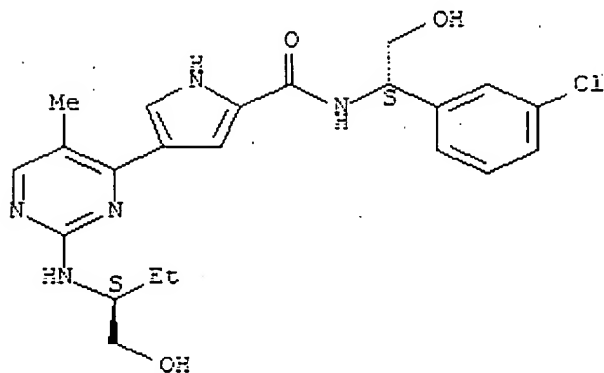
Claims 1-7, 9-12, and 14 rejected under 35 U.S.C. 103(a) as being obvious over Cao et al. (WO 2002/64586) in view of In re Wood (199 USPQ 137).



The instant invention is drawn to the compound and its pharmaceutical composition.

Determination of the scope and content of the prior art (MPEP §2141.01)

Cao et al. teach a compound of the formula



See Example 232, page 137. Cao et al.

also teaches pharmaceutical compositions including the antiproliferative drug taxol.

See pages 20-28.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

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Cao et al. do not teach a hydrogen in the 5 position of the pyrimidine ring or methyl groups on the unsubstituted carbons of the pyrrole ring.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

Hydrogen and methyl are deemed obvious variants. In re Wood, 199 USPQ 137

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to follow the synthetic scheme of Cao et al. and substitute methyl for hydrogen where needed in the pyrimidine and pyrrole rings to make the claimed invention with a reasonable expectation of success. The motivation to do so is provided by Cao et al. Cao et al. teach the use of the synthesized compounds and compositions to treat cancer. See column 10, line 5 through column 13, line 50.

Thus, the claimed invention as a whole was *prima facie* obviousness over the combined teachings of the prior art.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

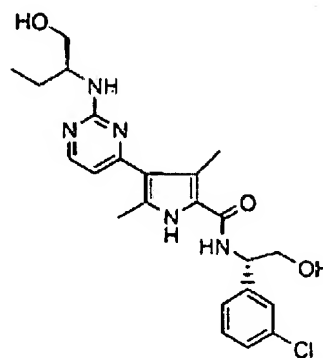
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to

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be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

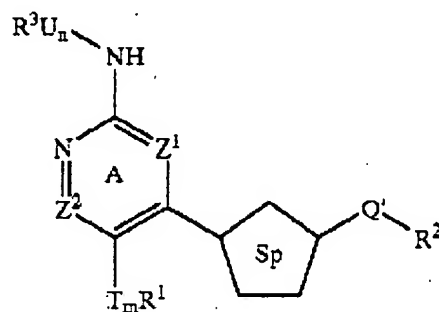
Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-7, 9-12, and 14 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2 and 22-23 of U.S. Patent No. 6,743,791 in view of In re Wood (199 USPQ 137).



The instant invention is drawn to the compound and its pharmaceutical composition.

Determination of the scope and content of the prior art (MPEP §2141.01)



'791 teaches a compound of the formula with substitutions as defined. '791 also teaches pharmaceutical compositions including an antiproliferative agent.

Ascertainment of the difference between the prior art and the claims (MPEP

§2141.02)

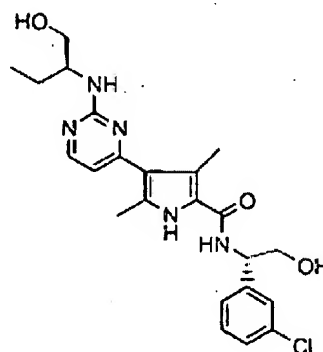
'791 does not allow for two methyl groups on the unsubstituted carbons of the pyrrole ring.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

Hydrogen and methyl are deemed obvious variants. In re Wood, 199 USPQ 137

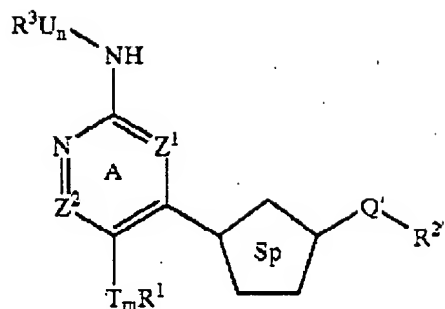
Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to follow the synthetic scheme of '791 and substitute methyl for hydrogen where needed in the pyrrole ring to make the claimed invention with a reasonable expectation of success. The motivation to do so is provided by '791 '791 teaches the use of the synthesized compounds and compositions to treat cancer.

Claims 1-7, 9-12, and 14 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 20 and 41-42 of copending Application No. 10/770,814, published as US-PGPUB 2004/0229875 A1 in view of In re Wood (199 USPQ 137) and Patani et al. (*Chemical Reviews* 1996, 3147-3176).



The instant invention is drawn to the compound and its pharmaceutical composition.

Determination of the scope and content of the prior art (MPEP §2141.01)



'814 teaches a compound of the formula with substitutions as defined. '814 also teaches pharmaceutical compositions including an antiproliferative agent.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

'814 does not allow for two methyl groups on the unsubstituted carbons of the pyrrole ring or nitrogen in the Z1 position.

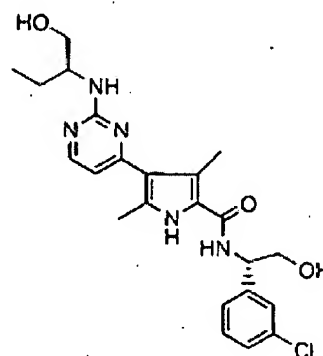
Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

Hydrogen and methyl are deemed obvious variants. In re Wood, 199 USPQ 137 Patani et al. teach the bioisosteric replacement of nitrogen for carbon in a six membered aryl ring. See Figure 39 and Table 30 on page 3160.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to follow the synthetic scheme of '814, substitute methyl for hydrogen where needed in the pyrrole ring, and substitute nitrogen for carbon in the Z1 position to make the claimed invention with a reasonable expectation of success. The motivation to do so is provided by '814 '814 teaches the use of the synthesized compounds and compositions to treat cancer.

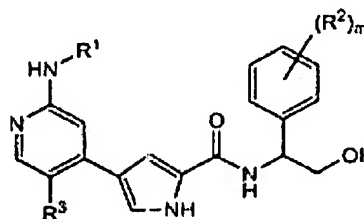
This is a provisional obviousness-type double patenting rejection.

Claims 1-7, 9-12, and 14 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 22-23 of copending Application No. 11/128,870, published as US-PGPUB 2006/0106069 A1 in view of In re Wood (199 USPQ 137) and Patani et al. (*Chemical Reviews* 1996, 3147-3176).



The instant invention is drawn to the compound and its pharmaceutical composition.

Determination of the scope and content of the prior art (MPEP §2141.01)



'870 teaches a compound of the formula with substitutions as defined. '870 also teaches pharmaceutical compositions including an antiproliferative agent.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

'870 does not allow for two methyl groups on the unsubstituted carbons of the pyrrole ring or nitrogen to replace the unsubstituted carbon meta to the pyridyl nitrogen to create a pyrimidine ring.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

Hydrogen and methyl are deemed obvious variants. In re Wood, 199 USPQ 137

Patani et al. teach the bioisosteric replacement of nitrogen for carbon in a six membered aryl ring. See Figure 39 and Table 30 on page 3160.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to follow the synthetic scheme of '870, substitute methyl for hydrogen where needed in the pyrrole ring, and substitute nitrogen to replace the unsubstituted carbon meta to the pyridyl nitrogen to create a pyrimidine ring to make the claimed invention with a reasonable expectation of success. The motivation to do so is provided by '870 '870 teaches the use of the synthesized compounds and compositions to treat cancer.

This is a provisional obviousness-type double patenting rejection.

Conclusion

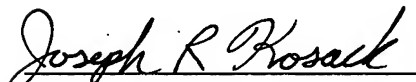
Claims 1-7, 9-12, and 14 are rejected. Claims 1-7, 9-12, and 14 are objected to.

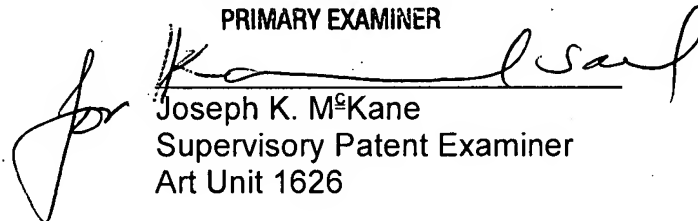
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Kosack whose telephone number is (571)-272-5575. The examiner can normally be reached on M-F 6:30 A.M. until 4:00 P.M. The examiner has every other Friday off.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph M^cKane can be reached on (571)-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Joseph Kosack
Patent Examiner
Art Unit 1626

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PRIMARY EXAMINER

Joseph K. M^cKane
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Art Unit 1626